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10/725,396	12/03/2003	Kazuhiro Takada	03500.017349.	2555
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FITZPATRICK CELLA HARPER & SCINTO 30 ROCKEFELLER PLAZA NEW YORK, NY 10112			MUMMERT, STEPHANIE KANE	
			ART UNIT	PAPER NUMBER

1637

DATE MAILED: 08/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

DETAILED ACTION

1. Applicant's election with traverse of Group 1, claims 1-8 and 19 in the reply filed on May is acknowledged. The traversal is on the ground(s) that there would not be undue burden in examining the two groups together. Specifically, Applicant asserts that "In the present instance, it is not believed that there would be an undue burden in examining the claims of Group I and II in a single application, since the two groups of claims are not so different as would require a burden on the examiner that is significantly beyond that of the normal burdens of examination" (p 2 of remarks). This is not found persuasive because as established in the previous restriction requirement, separate searches are required for the probe carrier product of group I and for the method of producing the probe carrier of group II. The product of group I may be formed using methods other than the method described in the claims of group II and therefore, in order to fully search the product would requires search terms that may not address the method of group II. Because separate searches of the prior art are necessary, to require a search of both of these inventions together does, indeed, pose and undue burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 9-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Election was made **without** traverse in the reply filed on May 22, 2006.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on January 28, 2004 was filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1 and 3-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Beebe et al. (US Patent 5,472,881; December 1995). Beebe teaches an investigation into methods of depositing DNA molecules onto a gold surface prior to scanning tunneling microscopy (STM) and/or atomic force microscopy (AFM) analysis (Abstract).

With regard to claim 1, Beebe teaches a probe carrier, characterized by comprising single-stranded DNA probe (col. 11, lines 45-60, where single stranded M13 template DNA was used to incorporate α -thio-nucleoside triphosphates for incorporation of a thiol group, and the double-stranded product was denatured to form single-stranded probes) immobilized to carrier having a thin film containing (111)-oriented single crystal gold formed thereon through sulfur

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atom (col. 7, line 8 to col. 8, line 60, where sulfur modified DNA probes were deposited on (111)-oriented single crystal gold (see col. 8, lines 35-38)).

With regard to claim 3, Beebe teaches a probe carrier according to claim wherein the sulfur atom interposed between the carrier and the single-stranded DNA probe is formed as a functional group of the single-stranded DNA probe (col. 7, lines 8-18 and lines 61-64, where a pentadecanucleotide with a sulfur group bonded to every phosphate atom was described; see also col. 11, lines 45-60, where the incorporation of α -thio-nucleoside triphosphates into a single strand probe is described).

With regard to claim 4, Beebe teaches an embodiment of claim 1, wherein the single-stranded DNA probe has a thiol group as functional group (col. 7, lines 8-18 and lines 61-64, where a pentadecanucleotide with a sulfur group bonded to every phosphate atom was described; see also col. 11, lines 45-60, where the incorporation of α -thio-nucleoside triphosphates into a single strand probe is described).

With regard to claim 5, Beebe teaches an embodiment of claim 1, wherein a method is used to apply the single-stranded DNA probe to the carrier upon immobilizing the single-stranded DNA probe to the carrier (col. 11, lines 45-60, where single stranded M13 template DNA was used to incorporate α -thio-nucleoside triphosphates for incorporation of a thiol group, and the double-stranded product was denatured to form single-stranded probes; col. 7, line 8 to col. 8, line 60, where sulfur modified DNA probes were deposited on (111)-oriented single crystal gold (see col. 8, lines 35-38). It is noted that this claim appears to represent a product-by-process claim).

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With regard to claim 6, Beebe teaches a carrier comprising a gold single crystal, wherein a method of deposition is used in forming the thin film containing the (111)-oriented single crystal gold (col. 7, line 8 to col. 8, line 60, where sulfur modified DNA probes were deposited on (111)-oriented single crystal gold (see col. 8, lines 35-38). It is noted that this claim appears to represent a product-by-process claim).

Regarding claims 5 and 6, it is noted that these claims appear to represent product-by-process claims. As noted in the MPEP § 2133, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In *Re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). There appears to be no structural change in the thin film or the immobilized probe(s) when the probe carrier is formed using the method(s) disclosed in the prior art, as compared to the probe carrier formed using ink-jet and/or immersion deposition methods as claimed. Therefore, the product produced in the prior art as described above is being viewed as having the same structure, and therefore anticipating, the probe carrier as claimed.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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7. Claims 1, 3-4 and 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meade et al. (US Patent 6,265,155; July 2001) in view of Rabke-Clemmer et al. (Langmuir, 1994, vol. 10, p. 1796-1800). Meade teaches solid supports with metallic surfaces comprising blocking moieties and modified nucleic acids for use in hybridization assays (Abstract).

With regard to claim 1, Meade teaches a probe carrier, characterized by comprising single-stranded DNA probe (col. 7, lines 9-18 and 28-35, where it is noted that probe nucleic acids are preferably single stranded nucleic acids) immobilized to carrier having a thin film containing gold formed thereon through sulfur atom (col. 7, line 63 to col. 8, line 54, where nucleic acids are modified with linker moieties comprising a sulfur atom, prior to attachment of the linker molecule to the metallic solid support; see also col. 3, lines 14-30, where it is noted that a preferred metallic support is covered in gold or copper, and methods of depositing gold are described).

With regard to claim 3, Meade teaches a probe carrier according to claim wherein the sulfur atom interposed between the carrier and the single-stranded DNA probe is formed as a functional group of the single-stranded DNA probe (col. 7, line 63 to col. 8, line 54, where nucleic acids are modified with linker moieties comprising a sulfur atom, prior to attachment of the linker molecule to the metallic solid support; see Formula 3, lines 25-38).

With regard to claim 4, Meade teaches an embodiment of claim 1, wherein the single-stranded DNA probe has a thiol group as functional group (col. 7, line 63 to col. 8, line 54, where nucleic acids are modified with linker moieties comprising a sulfur atom, prior to attachment of the linker molecule to the metallic solid support; see Formula 3, lines 25-38).

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With regard to claim 7, Meade teaches an embodiment of claim 1, wherein the thin film containing the gold is used as an electrode (col. 14, lines 15-56, Example 1, where hydroxythiol is attached to a gold electrode).

With regard to claim 8, Meade teaches an embodiment of claim 1, wherein the thin film gold can be applied with a voltage (col. 3, lines 27-30. where it is noted that the gold can be deposited onto any number of materials using multiple techniques, including electroplating).

Regarding claims 1, 3-4 and 8-7, Meade does not explicitly teach that the thin-film gold was (111)-oriented single crystal gold. Rabke-Clemmer teaches an investigation into methods of depositing DNA molecules onto a gold surface prior to scanning tunneling microscopy (STM) and/or atomic force microscopy (AFM) analysis, comprising the immobilization of DNA to (111)-oriented gold crystal (Abstract).

With regard to claim 1, 3-4 and 8-7, Rabke Clemmer teaches a thin film containing (111)-oriented single crystal gold (p. 1797, col. 1, 2nd paragraph; also p. 1797, col. 2, 'H₂S experiments' heading, where the Au(III) crystal was applied to the surface of the electrode/surface; p. 1797, 'sample preparation' heading and p. 1798, 'results and discussion' heading, where it is noted throughout that the Au(111) was a single crystal).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Meade to incorporate the thin-film containing (111) oriented single crystal gold of Rabke-Clemmer to arrive at the claimed invention with a reasonable expectation for success. As taught by Rabke-Clemmer, "Using the implications of Nuzzo and Allara's thiolated molecules adsorbed onto gold, we have investigated the adsorption properties of sulfur-modified DNA molecules on Au(111) surfaces. These

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modifications serve two purposes: (1) to aid in the adsorption of the DNA molecules to the substrate for subsequent STM/AFM imaging and (2) to provide a label for detection by electron spectroscopy” (p. 1796-1797). Furthermore, Rabke-Clemmer notes that “the choice of modified DNA oligomers was designed to enhance the chemisorption on the Au(111) single crystal, taking advantage of the sulfur-gold bonding demonstrated in the thiol-gold work of Nuzzo and Allara” (p. 1798, ‘results and discussion’ heading). Therefore, considering the related nature of the electrode described by Meade, which incorporates single stranded DNA probes on a surface coated by gold, in comparison to the adsorption of single-stranded DNA probes onto a (111)-oriented single crystal gold thin film, one of ordinary skill in the art at the time the invention was made would have been motivated to include the thin-film containing (111)-oriented single crystal gold taught by Rabke-Clemmer to the electrode of Meade with a reasonable expectation for success.

8. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beebe et al. (US Patent 5,472,881; December 1995) as applied to claims 1 and 3-6 above, and further in view of Hashimoto et al. (US Patent 4,924,490; May 1990). Beebe teaches an investigation into methods of depositing DNA molecules onto a gold surface prior to scanning tunneling microscopy (STM) and/or atomic force microscopy (AFM) analysis (Abstract).

Beebe teaches all of the limitations of claims 1 and 3-6 as recited in the 102 rejection stated above.

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With regard to claim 2, Beebe teaches a thin film containing (111)-oriented single crystal gold ((col. 7, line 8 to col. 8, line 60, where sulfur modified DNA probes were deposited on (111)-oriented single crystal gold (see col. 8, lines 35-38)).

Regarding claim 2, Beebe does not explicitly teach the surface unevenness of the film formed on the carrier. Hashimoto teaches the formation of an X-ray mirror and incorporates the formation of multiple layers and incorporating specific requirements regarding surface roughness (Abstract).

With regard to claim 2, Hashimoto teaches an embodiment of claim 1, wherein surface unevenness of the thin film containing crystal gold are 0.5 nm or less per μm^2 (col. 4, lines 22-47, where the evaluation of the smoothness of a thin film of gold is described and where it is noted that the surface roughness of the film was measured to be 4.7 Å, which is less than 0.5 nm).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the method of thin film deposition disclosed by Hashimoto to the method of fabrication of a gold probe which comprises immobilized DNA probes of Beebe to arrive at the claimed invention with a reasonable expectation for success. As taught by Hashimoto, "it becomes essentially required that the film surface on the mirror should possess high smoothness (e.g., several tens of angstroms or below in terms of its surface roughness)". Hashimoto is concerned specifically with "a view to solving the above-mentioned points of problem, and aims at providing an improved X-ray mirror and an improved method of its production, with which it becomes possible to widen the selective range of the materials to be used as the substrate and to manufacture the same without employing an special machining

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method” (col. 2, lines 9-16). While Hashimoto produces a thin film of very low surface roughness as part of the formation of an X-ray mirror, the teachings of Hashimoto are relevant to the teachings of Beebe and would have motivated one of ordinary skill in the art to consult the teachings of Hashimoto when optimizing the process of film formation. Considering that Beebe teaches that “herein is described a method of using gold-thiol monolayer chemistry to anchor nucleic acids for imaging by STM and AFM” (col. 4, lines 30-33) and considering the sensitivity of STM and AFM to surface topography, one of ordinary skill in the art would have been motivated to produce a single crystal gold film with as low a degree of surface roughness or unevenness as possible. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the vapor deposition technique taught by Hashimoto to the probe carrier of Beebe to achieve a high degree of surface smoothness prior to analysis by AFM and STM with a reasonable expectation for success.

9. Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beebe et al. (US Patent 5,472,881; December 1995) as applied to claims 1 and 3-4 above, and further in view of Seki et al. (US Patent 6,624,071; September 2003). Beebe teaches an investigation into methods of depositing DNA molecules onto a gold surface prior to scanning tunneling microscopy (STM) and/or atomic force microscopy (AFM) analysis (Abstract).

It is noted that it is unclear from Applicant’s disclosure whether the method of ink-jet deposition and/or immersion confer a structural change to the thin film and/or immobilized probes. Therefore, a rejection has been made as recited in the 102 rejection above and also herein through a rejection under 35 U.S.C. 103.

With regard to claim 5, Beebe teaches a single-stranded DNA probe immobilized to the carrier (col. 11, lines 45-60, where single stranded M13 template DNA was used to incorporate α -thio-nucleoside triphosphates for incorporation of a thiol group, and the double-stranded product was denatured to form single-stranded probes; col. 7, line 8 to col. 8, line 60, where sulfur modified DNA probes were deposited on (111)-oriented single crystal gold (see col. 8, lines 35-38)).

With regard to claim 6, Beebe teaches a carrier comprising a gold single crystal, thin film containing the (111)-oriented single crystal gold (col. 7, line 8 to col. 8, line 60, where sulfur modified DNA probes were deposited on (111)-oriented single crystal gold (see col. 8, lines 35-38)).

Regarding claims 5 and 6, Beebe does not teach the deposition of the single stranded DNA probe using an ink jet method and does not teach that the single crystal thin film is deposited through immersion of the carrier in a gold complex solution. Seki teaches a method for fabricating a thin film pattern (Abstract).

With regard to claim 5, Seki teaches an embodiment of claim 1, wherein an ink jet method is used to apply the probe to the carrier (col. 6, lines 45-50; col. 7, lines 20-32, where the inclusion of ink jet spotting is described, and while the ink jet was incorporated to deposit thin film gold, as established further below, it would have been obvious to apply the ink jet format to the deposition of any type of molecule, including probe DNA).

With regard to claim 6, Seki teaches an embodiment of claim 1, wherein a method in which the carrier is immersed in a gold complex solution to form a gold single crystal,

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thin film on the carrier is used as a method of forming the thin film (col. 5, lines 5-11; col. 6, lines 34-41; col. 6, lines 64-67, where the process of 'dipping' or immersing the carrier in a gold complex solution, termed 'organometallic complex' is described; col. 7, lines 6-8, where examples of the organometallic gold complexes are detailed).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the various teachings of Seki described above, including the incorporation of ink jet spotting to array components on a thin film and the use of dipping or immersion to coat the thin film to the carrier probe comprising a gold thin film and DNA probes of Beebe to arrive at the claimed invention with a reasonable expectation for success. Seki notes, "this invention provides a patterning method capable of forming a thin film pattern on a substrate with high adhesion" (col. 1, lines 54-59) and also teaches that "the dipping method can be conducted by dipping the substrate formed with the pattern into a solution containing a metallic compound to be allowed to stand at a temperature for a period of time" (col. 6, lines 64-67). While Beebe and Seki teach different methods of carrier fabrication, both describe methods that arrive at a gold thin film coating as described previously.

Considering the ink jet deposition method described by Seki, Seki notes that "As an ink composition, a metallic compound containing ink composition, which will be described later, is used to discharge a liquid drop of the ink composition onto the thiol-based coupling agent layer from an ink jet head by the ink jet method" (col. 7, lines 23-32). Seki also teaches that "Heat is not applied in the ink jet method. Ink jetting by piezo-driving can be preferably used" (col. 6, lines 48-50). While Seki teaches the inclusion of the ink jet method for the deposition of the metallic thin film, Seki also generally teaches that the ink jet format dispenses a liquid drop onto

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the substrate. Considering this teaching by Seki, it would have been obvious to one of ordinary skill in the art to modify the ink jet spotting technique to incorporate virtually any liquid for deposition onto the carrier surface, including single-stranded probe DNA as disclosed and immobilized by Beebe. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the dipping and ink jet spotting taught by Seki to the probe format disclosed by Beebe with a reasonable expectation for success.

10. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beebe et al. (US Patent 5,472,881; December 1995) as applies to claims 1 and 3-6 above and further in view of Keen et al. (US Patent 6,060,327; May 2000). Beebe teaches an investigation into methods of depositing DNA molecules onto a gold surface prior to scanning tunneling microscopy (STM) and/or atomic force microscopy (AFM) analysis (Abstract).

Beebe teaches the limitations of claims 1 and 3-6 as recited in the 102 rejection stated above.

With regard to claim 19, Beebe teaches a molecular device manufactured by using thin film containing (111)-oriented single crystal gold (col. 7, line 8 to col. 8, line 60, where sulfur modified DNA probes were deposited on (111)-oriented single crystal gold (see col. 8, lines 35-38)).

Regarding claim 19, Beebe does not explicitly teach that the single crystal gold can be part of an electrode or the inclusion of a molecular chain such as DNA interconnecting electrodes.

With regard to claim 19, Keen teaches a molecular device manufactured by interconnecting the electrodes by using a molecular chain typified by DNA (Figure 2, where the two faces of the electrode are interconnected by a DNA molecule; col. 7, line 44 to col. 8, line 51, where the detail of the electrode format is described, where there is a first region where the sensor includes sequence-specific single-stranded nucleic acid 'wires' having a first and second end; see also col. 12, line 38 to col. 13, line 22).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the teachings of Keen, including the use of a bridging oligonucleotide in an electrode format to the thin film probe of Beebe to arrive at the claimed invention with a reasonable expectation for success. As taught by Keen, "Importantly, no mediator is required in this sensor design, so electron transfer is direct and fast from headgroup to electrode. Further, because the polymer strands are commonly oriented, headgroups are optimally presented for sensing the desired analyte component" (col. 13, lines 16-22). These benefits stated by Keen, address the need in the art for "an improved sensor design that rapidly transfers electrons from headgroup redox reactions to an electrode, does not rely on redox relay such as freely diffusing mediators, and optimally orients the headgroup with respect to the analyte" (col. 6, lines 43-47).

While the probe carrier format disclosed by Beebe does not orient the DNA probe molecules in the same manner as that described by Keen in the electrode format disclosed, Keen also addresses the issue of adsorbing a thiol-modified DNA molecule to a gold electrode substrate. As stated by Keen, "Another example is of a sequence-specific DNA sensor. A specific sequence of a single-strand DNA (nonconducting or insulating form) with 5' or 3'

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terminus thiol could be adsorbed to a gold electrode substrate" (col. 26, lins 51-57). Therefore, considering the teachings by Beebe and by Keen, and the directly stated motivation to incorporate a gold electrode substrate and a thiol-modified DNA probe, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the teachings of Keen, including the use of a bridging oligonucleotide in an electrode format to the thin film probe of Beebe to achieve an electrode which does not rely on redox mediators, with a reasonable expectation for success.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Tour et al. (J. Am. Chem. Soc., 1995, vol. 117, p. 9529-9534) discloses studies of the formation of self-assembled monolayers and multilayers on gold surfaces of oligomers that have a variety of thiol containing end groups. Toben et al. (US Patent 6,383,269; May 2002) discloses electrolyte compositions useful for forming gold coatings on substrates. Nakamura et al. (US Patent 6,495,328; December 2002) discloses a substrate for detecting base sequences that comprise a thin metal film and the immobilization of a nucleic acid polymer.

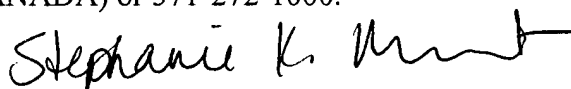
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

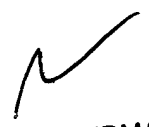
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Stephanie K Mummert, Ph.D.
Examiner
Art Unit 1637

SKM


JEFFREY FREDMAN
PRIMARY EXAMINER
7/25/02